REMARKS

After entry of this amendment, claims 1-13, 16-21, 25 and 27-32 are pending, of which claims 1, 6-13, 16-21, 25 and 27-30 are withdrawn. Claims 14 and 15 have been cancelled without prejudice or disclaimer. The claims have been amended without prejudice or disclaimer to delete the non-elected subject matter, to correct antecedent basis, to better comply with U.S. practice, and to address various points made in the Office Action, and find support *inter alia* in the original claims. Claim 2 finds further support in the specification at page 20, line 35, through page 21, line 6, page 77, lines 7-12, and page 81, lines 13-18. New claims 31 and 32 have been added. Support for the new claims is found in the original claims and in the specification at page 77, lines 7-12, and page 81, lines 13-18. No new matter has been added.

Applicants submit herewith a revised Sequence Listing which conforms to 37 CFR §§ 1.821-1.825 *via* EFS-Web, and a Statement to Support Filing and Submission in Accordance with 37 CFR §§ 1.821-1.825. The sequence contained in Figure 1 that was not included in the Sequence Listing as originally filed is now included in the revised Sequence Listing. Support for the amendments made to the Sequence Listing is found in the original Sequence Listing and in Figure 1 of the specification. Furthermore, the paragraph directed to the incorporation of the Sequence Listing in the specification which had been added in the First Preliminary Amendment dated January 31, 2003 has been replaced. No new matter has been added to the Sequence Listing or the specification. Entry of this Sequence Listing into the application is requested.

Objections to the Specification

The Examiner objects to the title of the invention and the abstract as being not descriptive. The title of the invention and the abstract has been amended as suggested by the Examiner. No new matter has been added.

The Examiner further rejects to the specification for containing hyperlinks. The hyperlinks found at pages 64 and 173 have been deleted. It is noted that the information referenced in the hyperlinks is available in the art and is referenced in the articles cited in the specification.

Moreover, section titles have been added into the specification, including a section entitled "BRIEF DESCRIPTION OF THE DRAWINGS" providing a brief description to Figure

1. Support for the description of Figure 1 can be found at page 131, lines 4-5, and Figure 1. The sequences recited in Figure 1 have also been identified by their corresponding sequence identifiers to comply with 37 CFR § 1.821(a) and (d). The sequences have also been included in the revised Sequence Listing submitted herewith. No new matter has been added.

In light of the amendment, it is believed that the objections are rendered moot. Reconsideration and withdrawal of the objections is respectfully requested.

Claim Objections

The Examiner objects to claims 2-5 for containing informalities. Claim 2 has been amended without prejudice or disclaimer to delete the non-elected subject matter. Applicants believe that the objection is rendered moot in view of the present amendment.

Claim Rejections – 35 USC § 112, First Paragraph

The Examiner rejects claims 2-5 for allegedly failing to comply with the written description requirement. The Examiner asserts that the term "fine chemicals" is broadly defined in the specification to encompass any type of chemical molecule in an organism. The Examiner further alleges that the specification does not describe the actual production of any type of chemical molecule in any type of organism in which the expression of SEQ ID NO: 1 is increased or generated. Additionally, the Examiner also asserts that the specification does not describe any nucleotide sequence encoding homologues or variants of SEQ ID NO: 2. Applicants respectfully disagree. However, to expedite prosecution, the claims have been amended without prejudice or disclaimer to recite the nucleic acid molecule used as well as the fine chemical produced in the claimed process with more specificity. Applicants respectfully request reconsideration in light of the present amendment and for the following reasons.

The "written description" requirement under 35 U.S.C. § 112, first paragraph, serves both to satisfy the inventor's obligation to disclose the technologic knowledge upon which the patent is based, and to demonstrate that the patentee was in possession of the invention that is claimed. *Capon v. Eshhar*, 418 F.3d 1349, 1357, 76 USPQ2d 1078, 1084 (Fed. Cir. 2005); *see also* MPEP § 2163. Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of structural chemical formulas that show that the invention was complete, or by

describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. *See* MPEP § 2163 (citation omitted).

A written description of an invention involving a nucleic acid, like a description of a chemical genus, "requires a precise definition, such as by structure, formula, [or] chemical name," of the claimed subject matter sufficient to distinguish it from other materials. *Fiers v. Revel*, 984 F.2d 1164, 1171 (Fed. Cir. 1993). For a claimed genus, the written description requirement may be satisfied through sufficient description of a representative number of species by actual reduction to practice, by disclosure of relevant identifying characteristics, by functional characteristics coupled with known or disclosed correlation between function and structure, or by a combination of such identifying characteristics. *See Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997). However, the determination of what is required to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter. *Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005).

It is noted initially that claim 2 is not directed to a nucleic acid but rather to a process, a process for the production of fine chemical comprising increasing or generating the expression of a nucleic acid encoding a ras-like GTPase (i.e. SEQ ID NO: 2 and homologues and variants thereof) in an organism or parts thereof. As in Example 16 of the Written Description Guidelines (Revision of March 25, 2008), the novelty resides in the method steps and not in the nucleic acids encoding ras-like GTPases. Furthermore, many ras-like GTPases are known in the art as in Example 16. Accordingly, the specification should satisfy the written description for amended claim 2 based on analogy to the examples in the Written Description Guidelines.

Furthermore, the specification provides relevant identifying characteristics of the sequences sufficient to distinguish a ras-like GTPase from other materials. As depicted in Figure 1, conserved regions or domains among ras-like GTPases derived from various organisms, including SEQ ID NO: 2, have been identified. For example, the conserved region represented by SEQ ID NO: 48 starts with the first box (doted line) and ends with the sixth box (doted line) as identified at the first sheet of Figure 1. Similarly, the region between the seventh and ninth

boxes (doted lines), together with the amino acid residue that locates before and after the doted line, respectively, represents another conserved region identified as SEQ ID NO: 50. Other conserved regions have also been identified, as shown in Figure 1. As stated in the specification at page 20, lines 16-20, polypeptides comprising the consensus sequences identified, including SEQ ID NO: 48 and 50, confer an increase of the production of fine chemicals. Thus, the genus of molecules has common structure which a skilled artisan would recognize.

Still further, functional homologues and variants of SEQ ID NO: 2 are described in the specification, for example at pages 71-72 and 83, which include natural variations, such as allelic variants or polymorphisms, which can lead to alterations in the amino acid sequences within a population without altering the functional activity of the ras-like GTPase represented by SEQ ID NO: 2. Accordingly, the claim includes the use of the expected range of natural variants, which are certainly within the scope of the invention as the skilled person would envision.

In addition, the specification shows, by way of working examples, that the claimed process results in production of fine chemicals in plants when using a nucleic acid encoding a ras-like GTPase (an actual reduction to practice). See Specification at page 189, lines 8-25 (Example 13) and Table 1 at page 174. As summarized in Table 1, where Cols. 3 and 4 provide the ratio of the fine chemicals analyzed between the transgenic and wild-type plants, it is clear that Arabidopsis plants overexpressing YNL090W (i.e. SEQ ID NO: 2) showed an increase in the production of at least 22 fine chemicals. Accordingly, contrary to the Examiner's assertion, the specification describes the actual production (reduction to practice) of fine chemicals in plants.

Because the specification provides relevant identifying characteristics of the sequences sufficient to distinguish a ras-like GTPase from other materials and many examples are known in the art, and because the specification provides a description of an actual reduction to practice, the specification provides adequate written description for the present claims as amended. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 2-5 are rejected under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential steps. Applicants respectfully disagree. However, in order to expedite prosecution, claim 2 has been amended without prejudice or disclaimer to include a further step

of growing the organism to produce the fine chemical. It is further noted that methods for increasing or generating expression of a nucleic acid in an organism are well known in the art and routinely employed by one skilled artisan. Such methods are also described in the specification at pages 21-25. Accordingly, it is respectfully submitted that the claims as amended is sufficiently clear and definite in view of the knowledge of the art as well as the disclosure of the specification. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. § 102(b)

Claims 2, 3 and 5 are rejected under 35 U.S.C. § 102(b) as being anticipated by Qadota et al. (hereinafter "Qadota"). Applicants respectfully disagree.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegall Bros., Inc. v. Union Oil Co.*, 814 F.2d 628, 631 (Fed. Cir. 1987).

The Examiner contends that Qadota teaches increasing or generating the expression of SEQ ID NO: 1 in yeast and recovering a free or bound fine chemical (i.e. the RAS2 protein), which anticipates the present claims. Applicants disagree. However, in order to expedite prosecution, claim 2 has been amended without prejudice or disclaimer to specify that the fine chemicals produced by the claimed process are selected from amino acids, carbohydrates, vitamins, organic acids, fatty acids, and carotinoids. Because a protein, by its very definition, is not an amino acid, a carbohydrate, a vitamin, an organic acid, a fatty acid, or a carotinoid, Qadota does not anticipate the claims as now amended. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. § 103(a)

Claim 4 is rejected under 35 U.S.C. § 103(a) as being obvious over Qadota in view of Monaghan *et al.* (hereinafter "Monaghan"). Applicants respectfully disagree and traverse the rejection for the following reasons.

To support a *prima facie* conclusion of obviousness, the prior art must disclose or suggest all the limitations of the claimed invention. See *In re Lowry*, 32 F.3d 1579, 1582, 32 USPQ2d 1031, 1034 (Fed. Cir. 1994); see also *Ex parte Alexander*, 86 USPQ2d 1120, 1122 (BPAI 2007)

(where the Board reversed an obviousness rejection in part because the Examiner had not identified all the elements of the claim in the cited prior art).

The Examiner relies on Qadota for teaching increasing or generating the expression of SEQ ID NO: 1 in yeast and recovering a free or bound fine chemical, i.e., a protein. The Examiner acknowledges that Qadota does not teach the limitations recited in claim 4, but relies on Monaghan for such teaching. As amended, the claims now require that the fine chemicals be at least one of amino acids, carbohydrates, vitamins, organic acids, fatty acids, or carotinoids. As discussed above, Qadota does not teach a process for the production of such fine chemicals. Because the reliance on Monaghan is that it teaches the steps recited in claim 4, it follows that the combination of Qadota and Monaghan does not render the present invention obvious because the combined teaching does not teach or suggest the production of the specific fine chemicals as now recited in the amended claim 2. Accordingly, it is respectfully submitted that Qadota and Monaghan, alone or in combination, does not render the claimed process obvious in view of the present amendment.

Moreover, it is noted that Qadota focuses on the effect of Rho2 gene product, a small GTP-bind protein, in the activation of geranylgeranyltransferase, a protein involved in post-translational protein prenylation. Monaghan, on the other hand, focuses on the effect of Lcb1 and Lcb2 gene products, homologues to the α-oxoamine synthases, in the serine palmitoyltransferase activity, a protein involved in sphingolipid synthesis. Because there is no connection between Rho2 and Lcb1/Lcb2 and their function in yeast, there is no motivation for one skilled in the art to combine these two references as suggested by the Examiner. For this additional reason, Qadota and Monaghan, alone or in combination, does not render the claimed process obvious.

Reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the above remarks and further in view of the above amendments, Applicants respectfully request withdrawal of the rejections and allowance of the claims.

Applicants reserve all rights to pursue the non-elected claims and subject matter in one or more divisional applications, if necessary.

This response is filed within the three-month period for response from the mailing of the Office Communication, to and including April 28, 2008. Applicants believe no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 03-2775, under Order No. 12810-00197-US from which the undersigned is authorized to draw.

Respectfully submitted,

By /s/ Hui-Ju Wu
Hui-Ju Wu, Ph.D.
Registration No.: 57,209
CONNOLLY BOVE LODGE & HUTZ LLP
1007 North Orange Street
P. O. Box 2207
Wilmington, Delaware 19899-2207
(302) 658-9141
(302) 658-5614 (Fax)
Agent for Applicants

#627423